L9 ANSWER 5 OF 12 MEDLINE
AN 96231648 MEDLINE
DN 96231648
TI Familial AL-amyloidosis in three Italian siblings.
AU Miliani A; Bergesio F; Salvadori M; Amantini A; Macucci M; Arbustini E; Becucci A; Sodi A; Zuccarini S; Menicucci A; Torricelli F; Capobianco T; Di Lollo S; Piazza E; Gemmi F; Cozzolino F; Merlini G
CS Institute of Internal Medicine IV, University of Firenze, Italy.
SO HAEMATOLOGICA, (1996 Mar-Apr) 81 (2) 105-9.
Journal code: FYB. ISSN: 0390-6078.
CY Italy
DT Journal; Article; (JOURNAL ARTICLE)
LA English
EM 199609
AB BACKGROUND AND METHODS. Familial occurrence of immunoglobulin-related (AL) amyloidosis has occasionally been reported. In this work we describe the concomitance of systemic amyloidosis and monoclonal gammopathy (one case of Waldenstrom's macroglobulinemia and two cases without multiple myeloma or related diseases) in three Italian siblings, two males and one female. RESULTS AND CONCLUSIONS. All of them showed a common pattern of polyneuropathy to different degrees; two presented a sicca syndrome and one also suffered from nephropathy. Two of them showed the same HLA typing with the same light chain type (k), but had different presenting symptoms. Polyneuropathy and a history of peptic disease in two cases was suggestive of type III familial amyloidotic polyneuropathy (FAP) occurring in the setting of a familial monoclonal component. However, immunohistochemical studies on different tissue specimens using anti-apolipoprotein A1 and anti-transthyretin antibodies were negative. Further screening of DNA samples for transthyretin (TTR) gene mutations was also negative. Clinical and laboratory investigations ruled out reactive or senile amyloidosis and immunohistochemical studies with anti-**light chain antibodies** on **amyloidotic** tissue specimens were positive. As a consequence, this family represents a new case of familial AL-am

L9 ANSWER 8 OF 12 MEDLINE
AN 93030471 MEDLINE
DN 93030471
TI Use of an anti-idiotypic monoclonal **antibody** in studying **amyloidogenic light chains** in cells, urine and fibrils: pathophysiology and clinical implications.
AU Bellotti V; Stoppini M; Perfetti V; Zorzoli I; Marinone G; Invernizzi R; Zambelli L M; Arbustini E; Grasso M; Ferri G; et al
CS Clinica Medica II, University Hospital Policlinico S. Matteo, Pavia, Italy..
SO SCANDINAVIAN JOURNAL OF IMMUNOLOGY, (1992 Oct) 36 (4) 607-15. Journal code: UCW. ISSN: 0300-9475.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199301
AB A monoclonal anti-idiotype antibody (IgG1k MoAb 3B11D4) raised against the amyloidogenic DEP lambda chain dimer binds a conformational idiotope also present on the monoclonal DEP IgA immunoglobulin. MoAb 3B11D4 does not recognize the reduced and alkylated lambda chain monomers, nor the 15-17-kDa fibrillar light chain fragments which have the same N-terminal sequence of the urinary light chains. The lack of about 70 amino acid residues of the C terminal of the protein prevents the formation of the self-limiting dimer and may facilitate the deposition of the fragments into amyloid fibrils. MoAb 3B11D4 recognizes the plasma cell clone in bone marrow and 9% of circulating B lymphocytes. Panning experiments demonstrate that this antibody has the capability to selectively eliminate the idiotype positive cells from peripheral blood. Antibodies with these characteristics could become a useful tool for better understanding the pathog

L18 ANSWER 3 OF 9 MEDLINE
AN 87129381 MEDLINE
DN 87129381
TI Monoclonal **anti-light chain** idiotype as a tumor-specific probe for human neoplastic B lymphocytes.
AU Wrightham M; Tutt A L; Glennie M J; Hamblin T J; Stevenson G T; Stevenson F K
SO BLOOD, (1987 Mar) 69 (3) 919-23.
Journal code: A8G. ISSN: 0006-4971.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 198706
AB Tumor cells from patients with B cell neoplasms often secrete small amounts of free monoclonal light chains that can be found in the urine. Such tumor-derived light chains of the lambda type from a patient with typical chronic lymphocytic leukemia have been used to raise mouse monoclonal **antibodies** (MoAbs). A hybridoma-secreting **antibody** that recognized the idiotypic lambda chain but not normal lambda chains by a preliminary screen but which also reacted with idiotypic IgM from the patient's tumor cells was selected. This MoAb in fact recognized 1 in 20 X 10(3) molecules of pooled normal lambda chains, thus establishing its specificity for a private idiotypic determinant. It failed to give a detectable reaction with normal IgM, normal serum, or a panel of IgM paraproteins. The **antibody** bound to the patient's neoplastic B cells but not to normal tonsillar cells. The site of binding of the **antibody** to idiotypic IgM is clearly separate from that of another MoAb specific for idiotypic determinants on heavy plus light chains, since the two showed additive binding curves. The determinant also appeared to be less available in dimeric lambda chains than in monomeric lambda chains or in idiotypic IgM. **Antibodies** to idiotypic determinants on light chains show some technical advantages and should be useful for monitoring and possibly **treating** B cell tumors, either alone or together with the more conventional anti-idiotypic **antibodies** that usually recognize the heavy and light chain

AN 89336697 MEDLINE
DN 89336697
TI Elimination of chemoresistant multiple myeloma clonogenic colony-forming cells by combined **treatment** with a plasma cell-reactive monoclonal antibody and a P-glycoprotein-reactive monoclonal antibody [published erratum appears in Cancer Res 1990 Jul 15;50(14):4451].
AU Tong A W; Lee J; Wang R M; Dalton W S; Tsuruo T; Fay J W; Stone M J
CS Cancer Immunology Research Unit, Charles A. Sammons Cancer Center, Baylor University Medical Center, Dallas, Texas 75246.
SO CANCER RESEARCH, (1989 Sep 1) 49 (17) 4829-34.
Journal code: CNF. ISSN: 0008-5472.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198911
AB Patients with multiple myeloma (MM) commonly become refractory to chemotherapy despite a favorable response to induction **treatment**. We examined the effectiveness of a previously characterized plasma cell-reactive monoclonal antibody, MM4, in eliminating MM clonogenic colony-forming cells (CCC) with a multidrug-resistant (MDR) phenotype. Experiments were performed using MM cell lines that exhibit 6 (RPMI 8226/DOX6)- and 40 (RPMI 8226/DOX40)-fold resistance to doxorubicin (DOX).

Both lines were selected from the chemosensitive MM line RPMI 8226/S and were cross-resistant to mitoxantrone, acronycine, etoposide, and vincristine. Surface marker analysis conducted in this study showed that DOX6 and DOX40 overexpressed the MDR1 gene product p170. Both MDR lines remained reactive to the plasma cell-reactive monoclonal **antibodies** MM4 and PCA-1 and expressed the relevant cytoplasmic **immunoglobulin light chain. Treatment** with MM4 and rabbit complement (C') was equally cytotoxic to RPMI 8226/S [80 +/- 5.6% (SD)], DOX6 [74 +/- 8.5], and DOX40 cells [75 +/- 11.3%], based on short-term chromium release studies. Furthermore, MM4 + C' deleted up to 3 logs of CCC colonies from chemosensitive and MDR lines (RPMI 8226/S, 99.87 +/- 0.11%; DOX6, 99.91 +/- 0.08%; DOX40, 99.55 +/- 0.44%). By comparison, the P-glycoprotein-reactive monoclonal antibody MRK-16 and C' inhibited tumor colony formation of MDR cells (8226/DOX6, 95.71 +/- 2.51%; 8226/DOX40, 99.61 +/- 0.43%) but affected that of chemosensitive cells only slightly (8.9 +/- 17.8%). In an attempt to optimize the depletion of myeloma CCC, MM4 was used together with MRK-16. This approach resulted in uniform depletion of myeloma clonogenic colony-forming cells from the chemosensitive (98.32 +/- 1.53%, n = 4) and MDR lines (8226/DOX6, 98.83 +/- 0.08%, n = 4; 8226/DOX40 99.29 +/- 0.62, n = 7) but did not result in enhanced CCC depletion. When DOX40 cells were mixed with normal bone marrow (BM) in the ratio of 90:10 (BM:MM), either MM4 or MRK-16 and C' depleted MM colonies (98.8 +/- 0.71% and 98.10 +/- 1.0%, respectively) without affecting the majority of BM progenitor cells.

These observations suggest that either MM4 or MRK-16 is useful for deplet

L15 ANSWER 3 OF 5 MEDLINE
AN 92371974 MEDLINE
DN 92371974
TI Localized **amyloidosis** of the lower genitourinary tract: a clinicopathological and immunohistochemical study of nine cases.
AU Khan S M; Birch P J; Bass P S; Williams J H; Theaker J M
CS Department of Histopathology, St. Mary's General Hospital, Portsmouth, UK..
SO HISTOPATHOLOGY, (1992 Aug) 21 (2) 143-7.
Journal code: GB4. ISSN: 0309-0167.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199211
AB A series of nine cases of localized **amyloidosis** of the lower genitourinary tract are reported. The patients comprised six males and three females with an age range of 50-79 years at initial presentation. Clinically and on cystoscopy, the lesions were often diagnosed as neoplasms. Histologically, seven cases had typical features of localized **amyloid** deposits, while two cases had an unusual appearance with a florid histiocytic and giant cell reaction. Using an immunoperoxidase staining method the deposits were non-reactive with **antibodies** to serum **amyloid** A protein, prealbumin and beta 2 microglobulin, while equivocal immunoreactivity was seen with **anti-**
ligh

L4 ANSWER 2 OF 6 MEDLINE
AN 1999244129 MEDLINE
DN 99244129 PubMed ID: 10229123
TI High affinity binding of **monoclonal antibodies** to the sequential epitope EFRH of beta-amyloid peptide is essential for modulation of fibrillar aggregation.
AU Frenkel D; Balass M; Katchalski-Katzir E; Solomon B
CS Department of Molecular Microbiology and Biotechnology, The George S. Wise Faculty of Life Sciences, Tel-Aviv University, Ramat Aviv, Israel.
SO JOURNAL OF NEUROIMMUNOLOGY, (1999 Mar 1) 95 (1-2) 136-42. Journal code: HSO; 8109498. ISSN: 0165-5728.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199905
ED Entered STN: 19990601
Last Updated on STN: 19990601
Entered Medline: 19990517
AB **Monoclonal antibodies** raised against the N-terminal of Alzheimer's beta-amyloid peptide (betaAP) were found to modulate its fibrillar aggregation. While mAbs 6C6 and 10D5 **inhibit** the **formation** of beta-**amyloid** fibrils, trigger disaggregation and reversal to its non-toxic form, mAb 2H3 is devoid of these properties. MAb 2H3 binds the sequence DAEFRHD, corresponding to position 1-7 of the betaAP with high affinity (2 x 10(-9) M) similar to its binding with the whole betaAP. The EFRH peptide strongly inhibits binding of mAbs 6C6 and 10D5 to betaAP, whereas it inhibits weakly the interaction of 2H3 with betaAP. Low affinity binding of mAb 2H3 to EFRH might explain its failure in prevention of beta-amyloid formation.

L10 ANSWER 15 OF 17 MEDLINE
AN 85106345 MEDLINE
DN 85106345
TI Variants of lymphoid lines produced with ricin A-chain monoclonal antibody
conjugates.
AU Lowe J A; Ling N R; Forrester J A; Cumber A J; Ross W C
SO JOURNAL OF IMMUNOLOGICAL METHODS, (1985 Jan 21) 76 (1) 93-104.
Journal code: IFE. ISSN: 0022-1759.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198505
AB Conjugates of ricin A-chain with monoclonal anti-**light chain antibodies** specifically killed cells hearing kappa or lambda **immunoglobulin** (Ig) **light chains.** Exposure of cells from B-lymphoblastoid cell lines (B-LCL) to conjugate for less than 30 h had only a slight effect on cell growth, but on 48 h exposure a marked killing effect was achieved. After recovery of growth, cells were re-exposed to conjugate for 9-14 days. **Treatment** of cells from the EB4 line (sIgG lambda) in this way yielded 4 variants which showed a marked reduction in levels of surface Ig lambda and secreted Ig lambda with slight, or no, reduction in MHC class II expression and similar growth rates to the parent line. Variant lines retained their phenotype over long periods of culture.

L10 ANSWER 10 OF 17 MEDLINE
AN 88271741 MEDLINE
DN 88271741
TI Expression of MHC class II antigens and immunoglobulins in immunized pig foetuses.
AU Trebichavsky I; Kovaru F; Nemec M
CS Institute of Microbiology, Czechoslovak Academy of Sciences, Praha..
SO FOLIA BIOLOGICA, (1988) 34 (1) 53-7.
Journal code: EYH. ISSN: 0015-5500.
CY Czechoslovakia
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198810
AB Pig foetal spleen, liver and thymus cells were examined by using polyclonal **antibody** to pig **immunoglobulins** and monoclonal **antibody** reacting with a **light chain** determinant of pig MHC class II antigens. Pig foetuses were immunized with flagellin on the 72nd day of prenatal life. On the 14th day following antigen **administration**, large numbers of class II antigen-bearing cells and Ig-containing cells were demonstrated in the spleen using the immunofluorescence technique. Topographical localization

L4 ANSWER 3 OF 6 MEDLINE
AN 97271379 MEDLINE
DN 97271379 PubMed ID: 9126330
TI A **monoclonal antibody** against acetylcholinesterase **inhibits** the **formation** of **amyloid** fibrils induced by the enzyme.
AU Reyes A E; Perez D R; Alvarez A; Garrido J; Gentry M K; Doctor B P; Inestrosa N C
CS Departamento de Biologia Celular y Molecular, Facultad de Ciencias Biologicas, Pontificia Universidad Catolica de Chile, Santiago, Chile.
SO BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1997 Mar 27) 232 (3) 652-5.
Journal code: 9Y8; 0372516. ISSN: 0006-291X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199705
ED Entered STN: 19970602
Last Updated on STN: 19970602
Entered Medline: 19970519
AB A **monoclonal antibody** (mAb) 25B1 directed against fetal bovine-serum acetylcholinesterase (FBS AChE) was used to examine the ability of the cholinergic enzyme to promote the assembly of amyloid-beta peptides (A beta) into Alzheimers fibrils. This mAb binds to the peripheral anionic site of the enzyme and allosterically inhibits catalytic activity of FBS AChE. Several techniques, including thioflavine-T fluorescence, turbidity, and negative-staining at the electron microscopy level, were used to assess **amyloid formation**. **Inhibition** of **amyloid formation** was dependent on the molar ratio AChE:mAb 25B1, and at least 50% of the inhibition of the AChE promoting effect occurs at a molar ratio similar to that required for inhibition of the esterase activity. Our results suggest that mAb 25B1 inhibits the promotion of the amyloid fibril formation triggered by AChE by affecting the lag period of the A beta aggregation process.

DN 93296472
TI Application of monoclonal anti-idiotypes in the study of AL amyloidosis: therapeutic implications.
AU Bellotti V; Stoppini M; Perfetti V; Zorzoli I; Marinone G; Maggi A; Invernizzi R; Arbustini E; Merlini G
CS Immunochemistry Laboratory, University Hospital IRCCS Policlinico S. Matteo, Pavia, Italy..
SO RENAL FAILURE, (1993) 15 (3) 365-71.
Journal code: RCG. ISSN: 0886-022X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199309
AB A monoclonal anti-idiotyped antibody (IgG1k MAb 3B11D4) has been raised against the lambda-chain dimers isolated from the urine of a patient (DEP) with **AL amyloidosis**. This **antibody** binds a conformational idiotope present on the monoclonal DEP IgA, but does not recognize the reduced and alkylated lambda-chain monomers, nor the 15- to 17-kDa **light** chain fragments obtained from the amyloid fibrils, which have the same N-terminal sequence as the urinary **light** chains. The nonreactivity of this MAb with amyloid fibrils was confirmed by immunohistochemical examination of cryostatic sections of an amyloidoma surgically removed from the patient's subcutaneous tissue. Our data demonstrate that the deletion of about 70 amino acid residues of the C-terminus of the lambda chain prevents the formation of the self-limiting dimer and may facilitate the deposition of fragments into amyloid fibrils.

With regard to the amyloidogenic clone, MAb 3B11D4 recognizes the plasma cell clone in bone marrow and 9% of circulating B lymphocytes. Panning and cytotoxicity experiments demonstrate that this antibody has the capability of selectively eliminating the idiotype-positive cells from peripheral blood. Antibodies with these properties could find application in a new therapeutic strategy which provides high-dose chemotherapy, total body irradiation, and rescue with circulating stem cells. These antibodies could be used in two distinct phases: first, in the purging of the stem cells to be infused from the amyloidogenic clone and, secondly, in an attemp

L2 ANSWER 1 OF 68 MEDLINE
AN 2000410029 MEDLINE
DN 20392583
TI Peripherally **administered antibodies** against **amyloid beta**-peptide enter the central nervous system and reduce pathology in a mouse model of Alzheimer disease.
AU Bard F; Cannon C; Barbour R; Burke R L; Games D; Grajeda H; Guido T; Hu K; Huang J; Johnson-Wood K; Khan K; Kholodenko D; Lee M; Lieberburg I; Motter R; Nguyen M; Soriano F; Vasquez N; Weiss K; Welch B; Seubert P; Schenk D; Yednock T
CS Elan Pharmaceuticals, 800 Gateway Boulevard, South San Francisco, California 94080, USA.. fbard@elanpharma.com
SO NATURE MEDICINE, (2000 Aug) 6 (8) 916-9.
Journal code: CG5. ISSN: 1078-8956.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200011
EW 20001101
AB One hallmark of Alzheimer disease is the accumulation of **amyloid beta**-peptide in the brain and its deposition as plaques. Mice transgenic for an **amyloid beta** precursor protein (APP) mini-gene driven by a platelet-derived (PD) growth factor promoter (PDAPP mice), which overexpress one of the disease-linked mutant forms of the human **amyloid** precursor protein, show many of the pathological features of Alzheimer disease, including extensive deposition of extracellular **amyloid** plaques, astrocytosis and neuritic dystrophy. Active immunization of PDAPP mice with human **amyloid beta**-peptide reduces plaque burden and its associated pathologies. Several hypotheses have been proposed regarding the mechanism of this response. Here we report that peripheral **administration** of **antibodies** against **amyloid beta**-peptide, was sufficient to reduce **amyloid** burden. Despite their relatively modest serum levels, the passively **administered antibodies** were able to enter the central nervous system, decorate plaques and induce clearance of preexisting **amyloid**. When examined in an ex vivo assay with sections of PDAPP or Alzheimer disease brain tissue, **antibodies** against **amyloid beta**-peptide triggered microglial cells to clear plaques through Fc receptor-mediated phagocytosis and subsequent peptide degradation. These results indicate that antibodies can cross the blood-brain barrier to act directly in the central nervous system and should be considered as a therapeutic approach for the treatment of Alzheimer disease and other

L9 ANSWER 1 OF 12 MEDLINE
AN 1999190074 MEDLINE
DN 99190074
TI Physicochemical consequences of amino acid variations that contribute to fibril formation by immunoglobulin light chains.
AU Raffen R; Dieckman L J; Szpunar M; Wunschl C; Pokkuluri P R; Dave P; Wilkins Stevens P; Cai X; Schiffer M; Stevens F J
CS Center for Mechanistic Biology and Biotechnology, Argonne National Laboratory, Illinois 60439, USA.
NC DK43757 (NIDDK)
GM16829 (NIGMS)
SO PROTEIN SCIENCE, (1999 Mar) 8 (3) 509-17.
Journal code: BNW. ISSN: 0961-8368.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199907
EW 19990702
AB The most common form of systemic **amyloidosis** originates from **antibody light chains**. The large number of amino acid variations that distinguish amyloidogenic from nonamyloidogenic light chain proteins has impeded our understanding of the structural basis of light-chain fibril formation. Moreover, even among the subset of human light chains that are amyloidogenic, many primary structure differences are found. We compared the thermodynamic stabilities of two recombinant kappa4 light-chain variable domains (V(L)s) derived from amyloidogenic light chains with a V(L) from a benign light chain. The amyloidogenic V(L)s were significantly less stable than the benign V(L). Furthermore, only the amyloidogenic V(L)s formed fibrils under native conditions in an in vitro fibril formation assay. We used site-directed mutagenesis to examine the consequences of individual amino acid substitutions found in the amyloidogenic V(L)s on stability and fibril formation capability. Both stabilizing and destabilizing mutations were found; however, only destabilizing mutations induced fibril formation in vitro. We found that fibril formation by the benign V(L) could be induced by low concentrations of a denaturant. This indicates that there are no structural or sequence-specific features of the benign V(L) that are incompatible with fibril formation, other than its greater stability. These studies demonstrate that the V(L) beta-domain structure is vulnerable to destabilizing mutations at a number of sites, including complementarity determining regions (CDRs), and that loss of variable domain stability is

L4 ANSWER 4 OF 6 MEDLINE
AN 96133955 MEDLINE
DN 96133955 PubMed ID: 8552659
TI **Monoclonal antibodies** inhibit in vitro fibrillar aggregation of the Alzheimer beta-amyloid peptide.
AU Solomon B; Koppel R; Hanan E; Katzav T
CS Department of Molecular Microbiology and Biotechnology, George S. Wise Faculty of Life Sciences, Tel-Aviv University, Ramat Aviv, Israel.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1996 Jan 9) 93 (1) 452-5.
Journal code: PV3; 7505876. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199602
ED Entered STN: 19960306
Last Updated on STN: 19960306
Entered Medline: 19960222
AB The beta-amyloid peptide, the hallmark of Alzheimer disease, forms fibrillar toxic aggregates in brain tissue that can be dissolved only by strong denaturing agents. To study beta-**amyloid formation** and its **inhibition**, we prepared immune complexes with two **monoclonal antibodies** (mAbs), AMY-33 and 6F/3D, raised against beta-amyloid fragments spanning amino acid residues 1-28 and 8-17 of the beta-amyloid peptide chain, respectively. In vitro aggregation of beta-amyloid peptide was induced by incubation for 3 h at 37 degrees C and monitored by ELISA, negative staining electron microscopy, and fluorimetric studies. We found that the mAs prevent the aggregation of beta-amyloid peptide and that the inhibitory effect appears to be related to the localization of the antibody-binding sites and the nature of the aggregating agents. Preparation of mAbs against "aggregating epitopes," defined as sequences related to the sites where protein aggregation is initiated, may lead to the understanding and prevention of protein aggregation. The results of this study may provide a foundation for using mAbs in vivo to prevent the beta-amyloid peptide aggregation that is associated with Alzheimer disease.